

LAF3 Rec'd PCT/PTO 30 NOV 2005

PTO-1390 (Rev.02-2005)

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

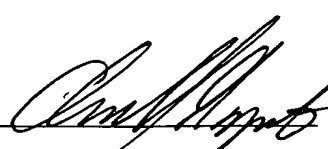
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| TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371 | | ATTORNEY'S DOCKET NUMBER VER-190XX |
| | | U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 10/532,512 |
| INTERNATIONAL APPLICATION NO. PCT/NL2003/000728 | INTERNATIONAL FILING DATE 27 October 2003 | PRIORITY DATE CLAIMED 25 October 2002 |
| TITLE OF INVENTION SYSTEM FOR EARLY DETECTION OF DISEASE AND DEVELOPMENT OF DISEASE-SPECIFIC BIOMARKERS | | |
| APPLICANT(S) FOR DO/EO/US Johannes Henricus Joseph van Nesselrooij, Robert-Jan Antonius Nicolaas Lamers, Jeroen de Groot, Nicole Verzijl | | |
| Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: | | |
| <p>1. <input type="checkbox"/> This is a FIRST submission of items concerning a submission under 35 U.S.C. 371.</p> <p>2. <input checked="" type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a submission under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.</p> <p>4. <input checked="" type="checkbox"/> The US has been elected (Article 31).</p> <p>5. <input type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))</p> <p>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</p> <p>b. <input type="checkbox"/> has been communicated by the International Bureau.</p> <p>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</p> <p>6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).</p> <p>a. <input type="checkbox"/> is attached hereto.</p> <p>b. <input type="checkbox"/> had been previously submitted under 35 U.S.C. 154(d)(4).</p> <p>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))</p> <p>a. <input type="checkbox"/> are attached herewith (required only if not communicated by the International Bureau).</p> <p>b. <input type="checkbox"/> have been communicated by the International Bureau.</p> <p>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</p> <p>d. <input type="checkbox"/> have not been made and will not be made.</p> <p>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p> <p>Items 11 to 20 below concern document(s) or information included:</p> <p>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</p> <p>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</p> <p>13. <input type="checkbox"/> A preliminary amendment.</p> <p>14. <input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</p> <p>15. <input type="checkbox"/> A substitute specification.</p> <p>16. <input type="checkbox"/> A power of attorney and/or change of address letter.</p> <p>17. <input type="checkbox"/> A computer readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821-1.825.</p> <p>18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4).</p> <p>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</p> <p>20. <input checked="" type="checkbox"/> Other items or information: (1) LETTER REGARDING NUMBER OF INDEPENDENT AND TOTAL CLAIMS IN APPLICATION; and (2) Copy of 371 FORMALITIES LETTER dated November 8, 2005.</p> | | |

This collection of information is required by 37 CFR 1.414 and 1.491-1.492. The information is required to obtain the USPTO to process an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Express Mail Number

EV 223331329 US

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| U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 10/532,512 | | INTERNATIONAL APPLICATION NO PCT/NL2003/000728 | | ATTORNEY'S DOCKET NUMBER VER-190XX | |
| The following fees have been submitted: | | | | CALCULATIONS PTO USE ONLY | |
| 21. <input type="checkbox"/> Basic national fee..... | | \$300.00 | | \$ | |
| 22. <input type="checkbox"/> Examination fee If International preliminary examination report prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4) | | \$100.00 | | \$ | |
| All other situations | | \$200.00 | | | |
| 23. <input type="checkbox"/> Search fee Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority | | \$100.00 | | | |
| International Search Report prepared and provided to the Office..... | | \$400.00 | | \$ | |
| All other situations..... | | \$500.00 | | | |
| TOTAL OF 21, 22 and 23 = | | | | \$ | |
| <input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250.00 for each additional 50 sheets of paper or fraction thereof. | | | | | |
| Total Sheets | Extra Sheets | Number of each additional 50 or fraction thereof (round up to a whole number) | RATE | | |
| - 100 = | / 50 = | | X \$250.00 | \$ | |
| Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(h)). | | | | \$ 130.00 | |
| CLAIMS | | NUMBER FILED | NUMBER EXTRA | RATE | |
| Total claims | | - 20 = | | X \$ 50.00 | \$ |
| Independent claims | | - 3 = | | X \$200.00 | \$ |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable) | | | | + \$360.00 | \$ |
| TOTAL OF ABOVE CALCULATIONS = | | | | \$ 130.00 | |
| <input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by 1/2. | | | | \$ | |
| SUBTOTAL = | | | | \$ 130.00 | |
| Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(l)). | | | | \$ | |
| TOTAL NATIONAL FEE = | | | | \$ 130.00 | |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property | | | | \$ | |
| TOTAL FEES ENCLOSED = | | | | \$ 130.00 | |
| 12/05/2005 GFREY1 00000130 10532512 01 FC:1617 130.00 DP | | | | Amount to be Refunded: | \$ |
| | | | | Amount to be Charged: | \$ |
| <p>a. <input checked="" type="checkbox"/> A check in the amount of \$ 130.00 to cover the above fees, except assignment recordation, is enclosed. Please also see enclosed LETTER REGARDING NUMBER OF INDEPENDENT AND TOTAL CLAIMS IN APPLICATION.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>23-0804</u>. A duplicate copy of this sheet is enclosed.</p> <p>d. <input type="checkbox"/> Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.</p> <p>NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.</p> | | | | | |
| <p>SEND ALL CORRESPONDENCE TO: _____ which is associated with the Law Firm of:</p> <p><input checked="" type="checkbox"/> Customer Number 00207</p> <p style="text-align: right;">WEINGARTEN, SCHURGIN, GAGNEBIN & LEOVICI LLP Ten Post Office Square Boston, Massachusetts 02109 United States Telephone: (617) 542-2290 Fax: (617) 451-0313</p> <p>Attorney Signature:  Date: <u>11-30-05</u></p> <p>Attorney Name: <u>Charles L. Gagnebin III</u> Registration No: <u>25,467</u></p> | | | | | |



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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| U.S. APPLICATION NUMBER NO. | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
| 10/532,512 | Johannes Henricus Joseph Van Nesselrooy | VER-190XX |

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| INTERNATIONAL APPLICATION NO. |
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PCT/NL03/00728

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|------------------|---------------|
| I.A. FILING DATE | PRIORITY DATE |
| 10/27/2003 | 10/25/2002 |

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WEINGARTEN, SCHURGIN, GAGNEBIN & LEOVICI LLP
 TEN POST OFFICE SQUARE
 BOSTON, MA 02109

CONFIRMATION NO. 7072

371 FORMALITIES LETTER



OC000000017412773

Date Mailed: 11/08/2005

NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495).

- Copy of the International Application filed on 04/25/2005
- Copy of the International Search Report filed on 04/25/2005
- Preliminary Amendments filed on 04/25/2005
- Information Disclosure Statements filed on 04/25/2005
- U.S. Basic National Fees filed on 04/25/2005
- Priority Documents filed on 04/25/2005
- Specification filed on 04/25/2005
- Claims filed on 04/25/2005
- Drawings filed on 04/25/2005

BY: RECEIVED
 NOV 10 2005
 WEINGARTEN, SCHURGIN,
 GAGNEBIN & LEOVICI LLP

The applicant needs to satisfy supplemental fees problems indicated below.

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Additional claim fees of **\$450** as a non-small entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.
- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date.
- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.492(h) of \$130 for a non-small entity, missing items identified in this letter.

Express Mail Number

EV 223331329 US

SUMMARY OF FEES DUE:

Total additional fees required for this application is **\$580** for a Large Entity:

- **\$130** Surcharge.
- Total additional claim fee(s) for this application is **\$ 450**
 - **\$400** for **2** independent claims over 3.
 - **\$50** for **17** total claims over 20.

ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

*A copy of this notice **MUST** be returned with the response.*

KAYA L LEWIS BALTIMORE

Telephone: (703) 308-9140 EXT 202

PART 1 - ATTORNEY/APPLICANT COPY

| U.S. APPLICATION NUMBER NO. | INTERNATIONAL APPLICATION NO. | ATTY. DOCKET NO. |
|-----------------------------|-------------------------------|------------------|
| 10/532,512 | PCT/NL03/00728 | VER-190XX |